

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference MXG/PB60615	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/EP2004/014076	International filing date (day/month/year) 09/12/2004	(Earliest) Priority Date (day/month/year) 12/12/2003
Applicant GLAXO GROUP LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

TRICYCLIC INDOLE HYDROXYETHYLAMINE DERIVATIVES AND THEIR USE IN THE TREATMENT OF ALZHEIMER'S DISEASE.

5. With regard to the abstract,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

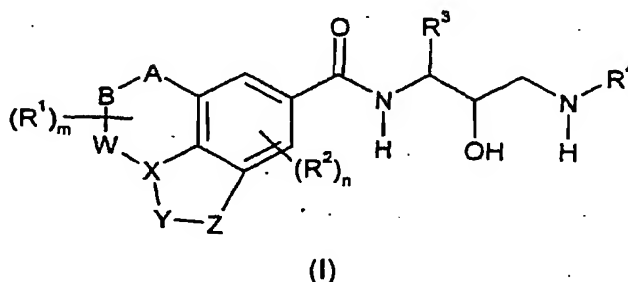
INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP2004/014076

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

The present invention relates to novel hydroxyethylamine compounds having Asp2 (β -secretase, BACE1 or Memapsin) inhibitory activity of formula I, processes for their preparation, to compositions containing them and to their use in the treatment of diseases characterised by elevated β -amyloid levels or β -amyloid deposits, particularly Alzheimer's disease.



wherein, *inter alia*;

A-B represents $-\text{NR}^5-\text{SO}_2-$ or $-\text{NR}^5-\text{CO}-$;

R^5 represents hydrogen, C_{1-6} alkyl, C_{3-6} alkenyl, C_{3-6} alkynyl, C_{3-10} cycloalkyl, $-\text{C}_{0-6}$ alkyl-aryl, $-\text{C}_{0-6}$ alkyl-heteroaryl, $-\text{C}_{0-6}$ alkyl-heterocyclyl, $-\text{C}_{3-10}$ cycloalkyl-aryl or $-\text{C}_{3-10}$ cycloalkyl-heteroaryl;

-W- represents $-\text{CH}_2-$, $-(\text{CH}_2)_2-$, $-(\text{CH}_2)_3-$, $-\text{C}(\text{H})=\text{C}(\text{H})-$ or $-\text{CH}_2-\text{C}(\text{H})=\text{C}(\text{H})-$;

X-Y-Z represents $-\text{C}=\text{CR}^6-\text{NR}^6-$;

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International Application No
PCT/EP2004/014076**A. CLASSIFICATION OF SUBJECT MATTER**
IPC 7 C07D513/06 A61K31/554 A61P25/28
//(C07D513/06,281:00,209:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHEDMinimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, PAJ, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	WO 2004/050619 A (GLAXO GROUP LIMITED; DEMONT, EMMANUEL, H; FALLER, ANDREW; MACPHERSON,) 17 June 2004 (2004-06-17) the whole document	1-8
P,X	WO 2004/094430 A (GLAXO GROUP LIMITED; DEMONT, EMMANUEL, HUBERT; REDSHAW, SALLY; WALTER,) 4 November 2004 (2004-11-04) the whole document	1-8
A	US 6 207 664 B1 (HAYWARD CHERYL M ET AL) 27 March 2001 (2001-03-27) the whole document	1-8
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

25 February 2005

Date of mailing of the international search report

10/03/2005

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International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01/70672 A (ELAN PHARMACEUTICALS, INC) 27 September 2001 (2001-09-27) cited in the application see the whole document, especially defintions of J or Rn and claim 26 -----	1-8
A	WO 98/33795 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA; KICK, ELLEN, K; ELLMAN, J) 6 August 1998 (1998-08-06) see whole document, especially defintions of R3 in claim 1. -----	1-8
A	WO 02/02505 A (ELAN PHARMACEUTICALS, INC) 10 January 2002 (2002-01-10) cited in the application see whole document. -----	1-8
A	WO 03/040096 A (ELAN PHARMACEUTICALS, INC; PHARMACIA & UPJOHN COMPANY; JOHN, VARGHESE;) 15 May 2003 (2003-05-15) cited in the application see defintions of Rn as (I) with X as C0 and Rn-1 as (B) -----	1-8
A	KOZIKOWSKI A P ET AL: "Chemistry, binding affinities, and behavioral properties of a new class of Antineophobic mitochondrial DBI receptor complex (mDRC) ligands" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 36, 1993, pages 2908-2920, XP002259612 ISSN: 0022-2623 See compound 9, Table 2 -----	1-8
A	TETRAHEDRON, vol. 50, no. 7, 1994, pages 2017-2028, XP002319196 See compounds 9 and 22 -----	1-8

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
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